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Docket No.: 7872-027-999 Serial No.: 08/487,355 Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

HIV1LAI (DP-178; SEQ ID NO.:1) YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF

HIV1SF2 (DP-185; SEQ ID NO.:3) YTNTIYTLLEESQNQQEKNEQELLELDKWASLWNWF

YTSLIYSLLEKSQTQQEKNEQELLELDKWASLWNWF YTGIIYNLLEESQNQQEKNEQELLELDKWANLWNWF HIVIRF (SEQ ID NO.:4) HIVIMN (SEQ ID NO.:5) LEANISKSLEQAQIQQEKNMYELQKLNSWDIFGNWF HIV2RÓD (SEQ ID NO.:6)

LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL HIV2NIHZ (SEQ ID NO.:7) SSESFTLLEQWNNWKLQLAEQWLEQINEKHYLEDIS DP180 (SEQ ID NO.:2)

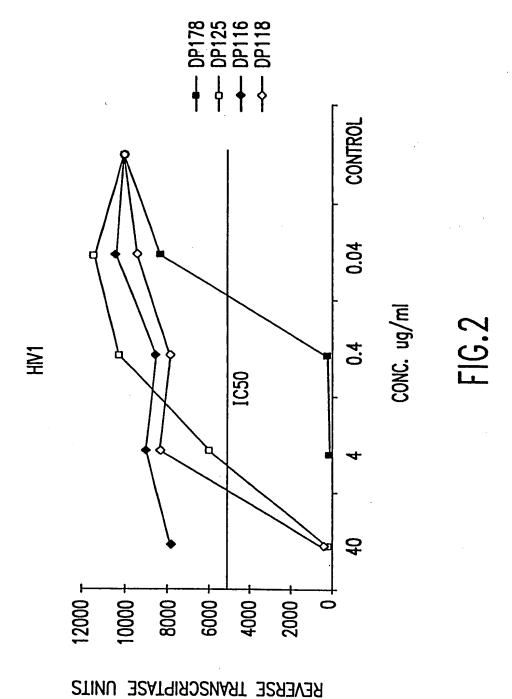
CGGNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQ QQLLDVVKRQQEMLRLTVWGTKNLQARVTAIEKYLKDQ (SEQ ID NO.:10)

DP118

(SEQ ID NO.:8) DP116 (SEQ ID NO.:9) DP125

LQARILAVERYLKDQQQ

Serial No.: 08/487,355



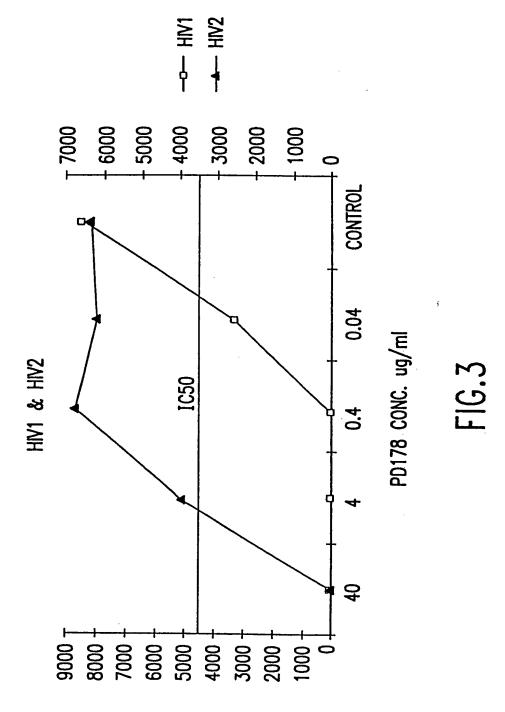
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Number	of Syn	c <u>y</u> lio,	/well	: conce	ntratio	n in μg/n	ml (micro	grams/ml)	
DP178	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
Syncylia HIV1LAI	0	0	0	0	0	0	0	0	67
HIVIMN	0	0	0	0	0	ND	ND	ND	34
HIVIRF	0	Ö	0	0	0	ND	ND	ND ND	65
HIV1SF2	0	Ö	0	0	0	ND	ND	ND	58
DP125	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
Syncytia	•	•							
HIVILAI	0	0	54	69	80	75	79	82	67
HIVIMN	0	0	30	36	ND	ND	ND	ND	34
HIVIRF	0	0	67	63	ND	ND	ND	ND	65
HIV1SF2	0	0	9	66	ND	ND	ND	ND	58
DP116	10	5	1	0.2	0.1	0.05	0.025	0.0125	Contro!
Syncytia									
HIVILAL	75	ND	ND	ND	ND	ND	ND	ND	67
HIVIMN	35	ND	ND	ND	ND	ND	ND	ND	34
HIVIRF	81	ND	ND	ND	ND	ND	ND	ND	65
HIV1SF2	81	ND -	ND	ND	ND	ND	ND	ND	58

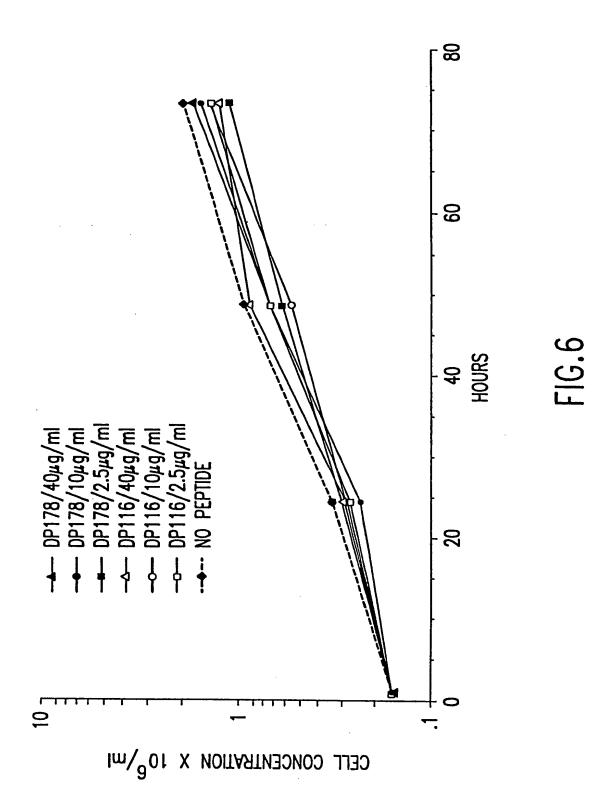
FIG.4A

DP180 Syncytia	40	20	10	5	2.5	1.25	0.625	0.3125	Control
HIVILAL	50	>45	>45	>45	>45	>45	>45	>45	58
DP185	40	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia HIV1LAI	0	0	0	0	0	0	0	ND	60

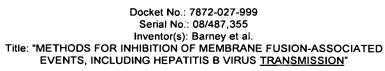
FIG.4B

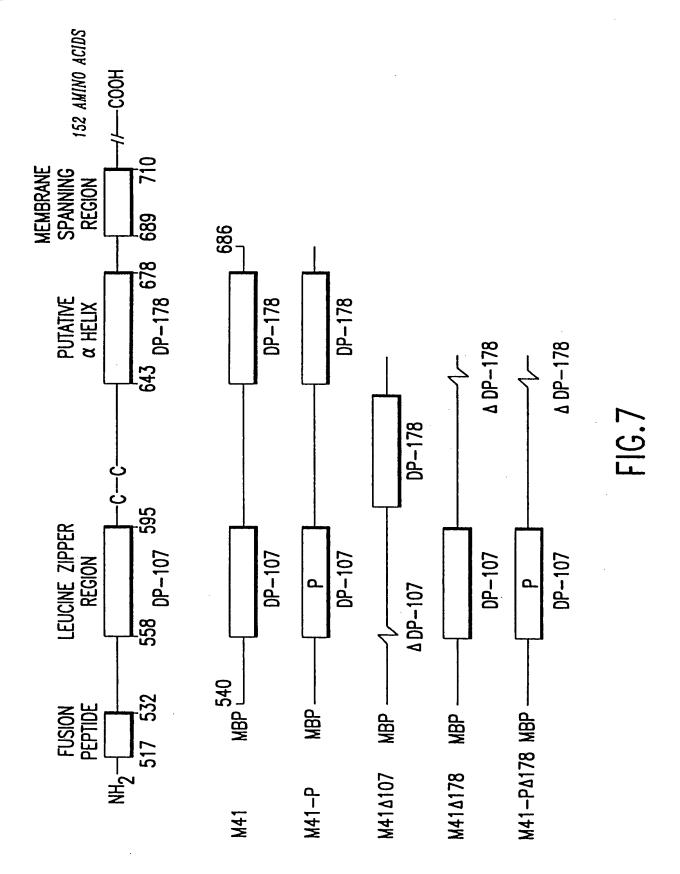


				HJV1				
_	Number	of	Syncyti	ia/well:	conce	ntration	in ng/ml	(nanograms/ml)
DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncylia HIV1	0	0	0	0	0	14	20	48
DP116	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncylia HIV1	ND	48	ND	ND	ND	ND	ND	ND
				H1V2				:
	Numb <u>er</u>	of	Syncyti	ia/well:	conce	ntration	in μg/ml	(micrograms/ml)
DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncylia HIV2	50	54	55	57	63	77	78	76
DP116	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncylia HIV2	ND	58	ND	ND	ND	ND	ND	ND

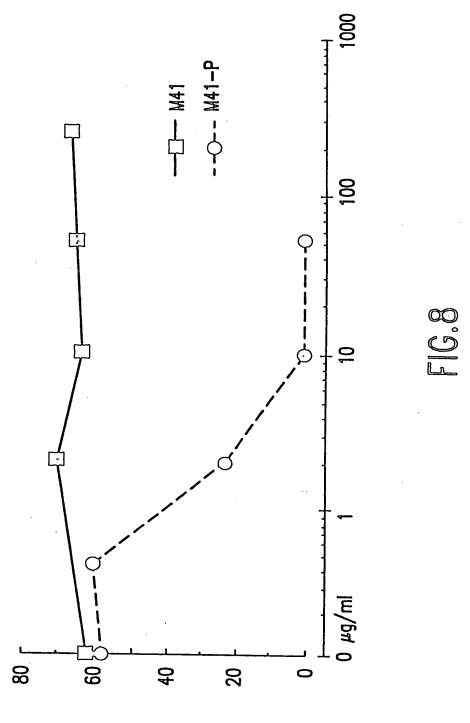


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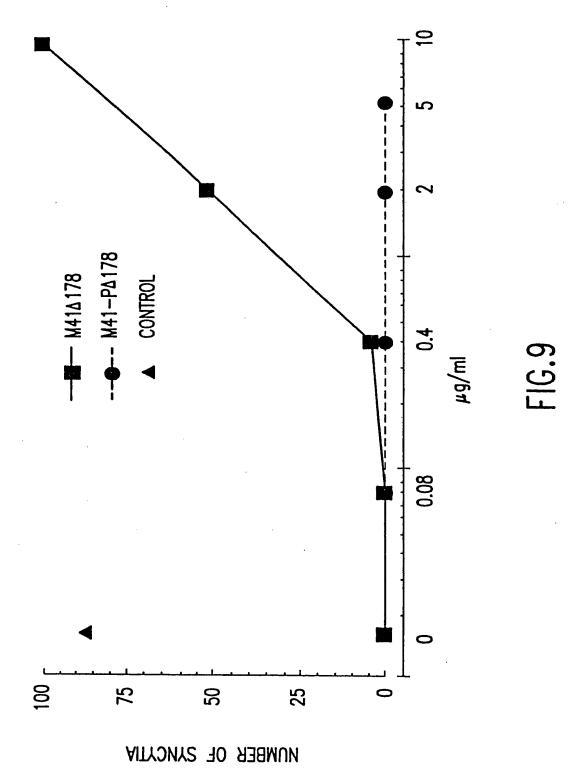


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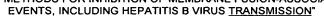
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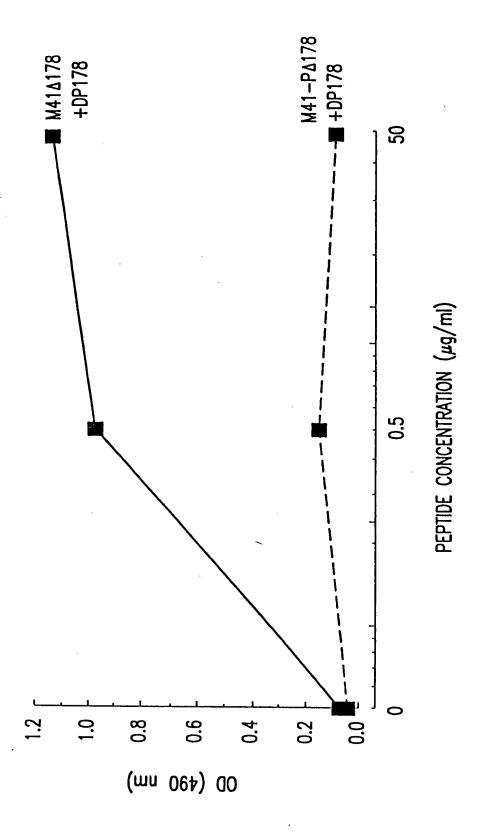
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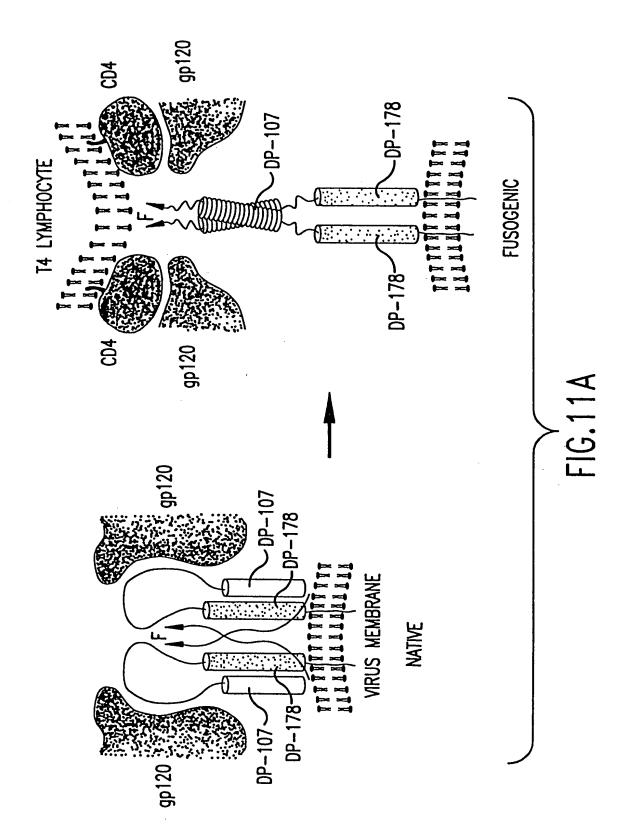


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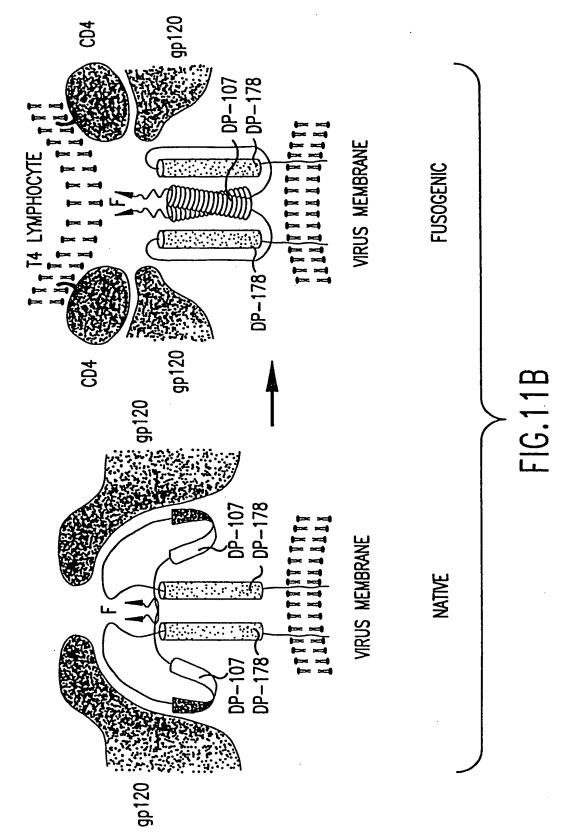
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FIG. 12



WOL I IS		[ILQT] {CFIMPSTY}	[ILQTV] {COF IMPST}	[ILQTV] {CDF IMPST}		[EKLNOV] {CFKMPS{	[EKLNOV] {CFKAPS}	[EKLQY] {ACFGMPRWMY}	[EKLONY] {CFGNPRVY}	[EFKLOWY] {CFGMPRVY}	[ETLNOSY] {ACFGMPRVMY}	[EILNOSHY] {CFGMPRVY}	[EFILNOSMY] {CFGMPRVY}
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	Sequence	GCN4 (gcn4 yeast)	0P-107 (env_hv1bru)L1=0 N N L L R A 11E A 0 0	OP-107 (env_hv1bru)L1=0	0P-107 (env_hv1bru)L1=0 N N L L R A 1 E A 0 0 1	DP-107 (env_hv1bru)L2=0	OP-107 (env_hv1bru)L2=0	0P-107 (env_hv1bru)L2=D N N L L R A I E A 0 0 H



Hybrid Motif				[EKLIANDWIY] {GFGIAP}	[EFKLIANOWY] {GFGAP}	[ILNOSY] {ACFGNPRVMY} [EILNANDSVY] {CFGNPM}	Y [EILLMADSVMY] (CFGMP)	M} [EFILMADSWM] {CFGMP}
Parent Molif		[LMNV] {CFGIMPTW}	[EKLQY] {ACFCMPRVMY}	[EKLCHY] {CFGHPRVY}	[EFKLOW] {CFGAPRVY}	[EILNOSY] {ACFGMPRW	[EILNOSWY] {CFGMPRVY} [EILMAGSWRY	[EFILNOSIM] {CFGMPRVY}
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	Sequence	GCN4 (gan4 yeast)	OP-178 (env_hv1bru)Y1=A	DP-178 (env_hv1bru)Y1=A	DP-178 (env_hv1bru)Y1=A	OP-178 (env_hv1bru)Y1=0	OP-178 (env_hv1bru)Y1=0	DP-178 (env_hv1bru)Y1=0



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Hybrid Molif		[CCIVILANTIMAY] {CCIVILA	[בנוערשאלוגעוו] (מיש ((0.10) [withten 1.00]	[EFILMACKSIVIT] {CFIRE}		(4)20) [200,000,000,000]	[EFKUMAQVMY] {CFM*}			[EFIKLMADSVMY] {CFMP}
Parent Motif		[LMAN] {CFGIMPTW} [ILQTV] {CDFIMPST}	[EFRLUMI] {CIUMANI}	[LMNV] {CFGIMPTW}	[ILQTV] {COF IMPST {	[EF ILNOSHY] {CFGMPRYY}	[LIANV] {CFGINPTW}	[EKLNOV] {CFIOAPS{	[EFKLOWY] {CFGAPRVY}	[LMAV] {CFGIMPTW}		
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	Sequence	GCN4 (gcn4 yeast) DP-107 (env_hv1bru)L1=D	DP-178 (env_hv1bru)Y1=A	GCN4 (gcn4 yeast)	DP-107 (env_hv1bru)L1=0	0P-178 (env_hv1bru)Y1=0	GCN4 (gcn4 yeast)	DP-107 (env_hv1bru)L2=0	DP-178 (env_hv1bru)Y1=A	GCN4 (aca4 venct)	0P-107 (env_hv1bru)L2=0	0P-178 (env_hv1bru)Y1=0



Docket No.: 7872-027-999 Serial No.: 08/487,355

Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

[AEFIKLMNORSTVMY] {GFP} : {COCHP} {GFP}

Hybrid Molif

Positions

(env_hv1bru)L1=0 env_hv1bru)L2=0 env_hv1bru)Y1=A env_hv1bru)Y1=0

Parent Motif K

Docket No.: 7872-027-999



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

EVENTS, INCLUDING HEPATTIS B VIRUS TRANSMISSION

Fusion

♥ALLMOTI5**♥**

Peptide

↑107x178x4↑

v...FLGFLG

A AGSTMGARSM TLTVQARQ ALL SGIVQQQ DP107-1

LRAIEAOOHL LOLTYWGIKO LOARILAYER YLKDO-DP107 QLLG★▼ I WGC

4107x178x44

♥ALLMOTI5♥

LVS Coilcd-Coil

SGKLICT TAVP ▼WNASWS NKSLEQIWNN MTWM *E ★WDREINN DP178-

YTSLIHSL IEESONOOEK NEOELLELDK* WASLWNWF-DP178 NI

◆ Transmembrane Region ◆

TNWLWYIK → IF IMIVGGLYGLRIVEAVLSIV NRVRQGYS → PL

+P23LZIPC+

SFQTHLPTPR GPDR *PEGIEE EGGERDRDRS IRLVNGSLAL IWDDLRSL* CL

♥ALLMOTI5♥

★107x178x4★

F *SYHRLRDLL LIVTRIVELL GRRGW *EALKY WWNLLQYWSQ

ELKNSAYSLL NAT ↑ AIAVAEG TDRVIEVVQG A ♥ CRAIRHIPR

RIRQGLERIL L



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

Fusion

♥ALLMOTI5**♥**

Peptide **▼....FLGFL** LGVGSAIAS GVA

♦ YSKYLIIL EGEYNKIKSA

+P1&12LZIPC+

LLSTNKAVVS LSNGVSVLTS KYLDLKNYID KQ♠♥ LL +PIVNKQ

4107x178x44

SC ASISNIETY I+ EFQQKNNRLLEITREFSYNAGA VITPVSTMLTNSELLSL

+P1&12LZIPC+

♥ALLMOTI5♥

INDM →PI →TNDQ KKLMSNNVQI V→ RQQSYSI→ MS IIKEEVLAYV

VQ♥ LPLYGVID TPCWKLHTSP LCTTNTKEGS NICLTRTDRG WYCDNAGSVS

FFPQAETCKV QSNRVFCDTM NSLTLPSEIN LCNVDIFNPK

YDCKIMTSKT DVSSSVITSL GAIVSCYGKT KCTASNKNRG

IIKTFSNGCDYVSNKGMDTV SVGNTLYYVN KQEGKSLYVK G

+P7, 12, & 23LZIPC+

★107x178x4★

♥ALLMOTI5**♥**

EPIINFYDPLVF +PSDE +FDASISOYNEKINOSLAF *I+ RKSDELL+

◆Transmembrane Region ◆

HNVNA + GK STTN + IMITTI IIVIIVILLS LIAVGLLLY + C+

KARSTPVTLS KDQLSGINNI AFSN



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

Fusion

Peptide

♥ALLMOTI5♥

4107x178x4 4

....FLGELG

▼AAGTA MGAAA ◆TALTYOSQILLAGILQQQKNLLAAY

4107x178x44

EAQ♠ QQM ♠LKLTIWGYKNLNARYTALEKYLEDQARLN♠ AWG♥ CA

LYS Coilcd-Coil

4107x178x44 ♥ALLMOTI5♥

WKOVCHTTVP WQWNNRTPDW ▼NNMT *WLE *WERQISYLEGNIT

+107x178x4

TOLEEARAOEEKNLD ↑ AYOKLSS* WSDFWSW ▼ FDF ASKWLN → ILK

◆Transmembrane Region ◆

IGFLDYLGIGLRLLYTY + YS + CIARVRQGYS PLSPQIHIHP WKGQPDNAEG

PGEGGDKRKN SSEPWQKESG TAEWKSNWCK RLTNWCSISS IWLYNS

♥ALLMOTI5♥

▼CLTL LVHLRSAFQY IQYGLGELKA AAQEAVVALA RLAQNAGYQIWL

ACRSAYRA IINSPRRVRQ GLEGILN

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

Fusion

4107x178x44

Peptide

♥ALLMOTI5**♥**

LVS_Coilcd-Coil

.....EAG

▼YYL

AGVALGVATA AQITAGIALIIQ **SNLNAQAIO

SLRTSLEQSNKAIEEIREATQETYIA* YOGYODY NONEL VP

▼ALLMOTI5 ▼

↑107x178x4↑

+P6 & 12LZIPC+

AMQHMSCELVGQRLGLRLLRYYTELLSIFGPSLRD *PISA **EISIQALIYAL

GGEHIKILEKLGYSGSD♠ MIAILESRGIKTKI♥ THVDLPGKF IILSISY

P1 & 12LZIPC

PTLSEVKGVIVHRLEAV SYNIGSQEWYTTVPRYIATNGYLISNFDESSCVFVS

ESAICSQNSL YPMSPLLQQC IRGDTSSCAR TLVSGTMGNK FILSKGNIVA

NCASILCKCY STSTIINQSP DKLLTFIASD TCPLVEIDGA TIQVGGRQYP

LVS Coiled-Coil

♥ALLMOTI5♥

+P12 & 23LZIPC+

DMVYEGKVAL G *PAISLD *RL*DVGTNLGNALKKLDDAKVLI*

+Transmembrane Region +

DSS+ NQILETYR RS ▼* SFN

FGSLL SYPILSCTAL ALLLLIYCC

K RRYQQTLKQH TKVDPAFKPD LTGTSKSYVR SL



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

Fusion ▼ALLMOTI5▼

Peptide

4107x178x44

▼......FIGAI IGSVALGVA TAAQITAASA LIQANQNAAN ◆ILRLKESITA

TIEAVHEYTDGLSQLAYA♠ VG KM♥ QQFVNDQFNNTAQELDCIKITQQV

♥ALLMOTI5**♥**

GVELNLYLTELTTV FGPQITSPAL *TQLTIQALYNAGGNMDYLLTKLGVG

P1 & 12LZIPC

LSVST TKGFASALVP KVVTQVGSVI EELDTSYCIE TDLDLYCTRI VTFPMSPGIY

SCLNGNTSAC MYSKTEGALT TPYMTLKGSV IANCKMTTCR CADPPGIISQ

♥ALLMOTI5♥

↑107x178x4↑

NYGEAVSLID RHSCN ★▼VLSLD GITLRLSGEF DATYQKNISI LDSQVIVTG

LVS Coiled-Coil

♦ Trans-

*N LDISTELGNY NNSISNALDK LEESNSKLDK VNVKLTSTSA + LIT

LIT* YL/

membrane Region +

<u>LTAISLVCGILSLV</u>♥♠ <u>LACYLMY</u>♦ KQKAQQKTLLWLGNNTLGQMRATTKM



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

Fusion

♥ ALLMOTI5 ♥

Peptide

↑107x178x4↑

LVS Coilcd-Coil

.....FFGGY

★IG ★TIALG *YATSAQITAAYALYEAKQARSDIEKLKE

<u> AIRDTNKAYOSYOS\$IGNLIYAIKSYQ* DYYNKE</u>♥♠ IVPSIARLGCEAAG

▼ALLMOTI5 **▼**

4107x178x44

LOLGIALTOH *YSELTNIFGDNIGSLOEKGIKLOGIASLYRTNITEY*

+P5 & 12LZIPC+

IFTTSTVDKYDIYDLLFTESIKVRVIDVDLNDYSITLQVRL *PLLTRLLNTQFYR

VDSISYNI# QNREWYI# PLPSHIMTKGAFLGGADVKECIEAFSSYIC

PSDPGFVLNHEMESCLSGNISQCPRTVVKSDIVPRYAFVNGGVVANCITT

TCTCNGIGNRINQPPDQGVKIITHKECNTIGINGMLFNTNKEGTLAFYTP

♥ALLMOTI5♥

4107x178x44

+P6 & 23LZIPC+

NDITLNNSVALD +PIDI +SIELN +KAKSDLEESKEWI+ RRSNQKL+

◆ Transmembrane Region ◆

DSIGNWHOSSTT

+IIIV + LIM HILFHNYT H+

IIAVKYY♥ R

IQKRNRVDQN DKPYVLTNK



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

Fusion Peptide

......GLEGAI AGFIENGWEGMIDGWYGFRHQNSEGTG

4107x178x44

♥ALLMOTI5♥

LVS Coilcd-Coil

*Q ◆AADLKST ◆QAAIDQINGKLNRVIEKTNEKFHQIEKEFSEVEGRIQ

DLEKYYEDTKIDL* WSYNAELLYALENQHTI♠ DLT♥ DSEMNKLFEKTR

RQLRENAEEMGNGCFKIYHKCDNACIESIRNGTYDHDVYRDEALNNRFQIKG

VELKSGYKDWILWISFAISCFLLCVVLLGFIMWACQRGNIRCNICI



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Docket No.: 7872-027-999

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\sqcup			[IC50 (XTT)	
	RSV F2	AV	(lm/bn)	C)
	T-142	#	39	‡
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	1-144	+	114	#
	1-145	#	40	+
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	1-149	-	336	•
	T-150	1	342	+
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	T-152	-/+	117	#
	T-153	ı	280	+
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AVG. 1C50	(XTT) UG/ML	>500	>500	>500	>500	>500	>500		165	26		>200	NOT TESTED	>500	>500	>500		>100	
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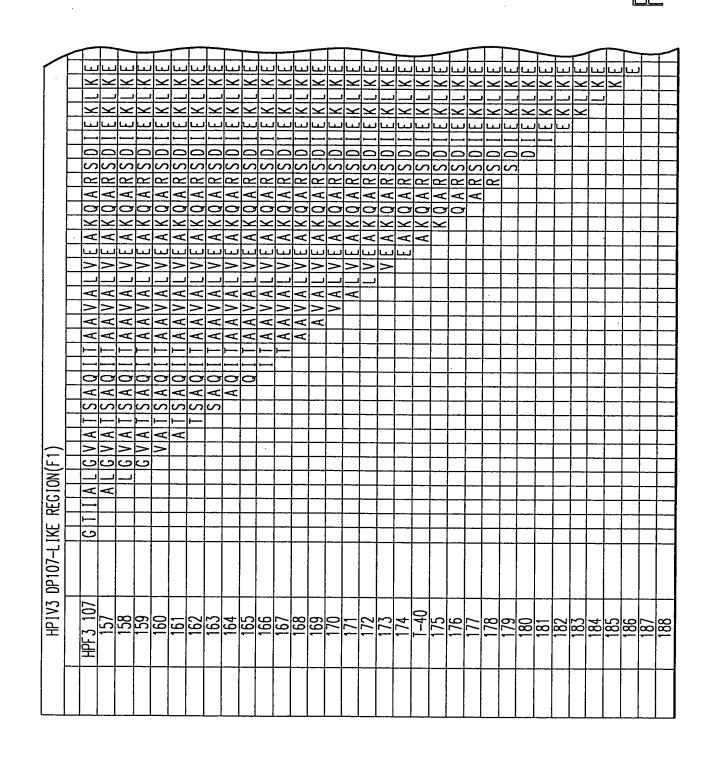


Docket No.: 7872-027-999

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Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

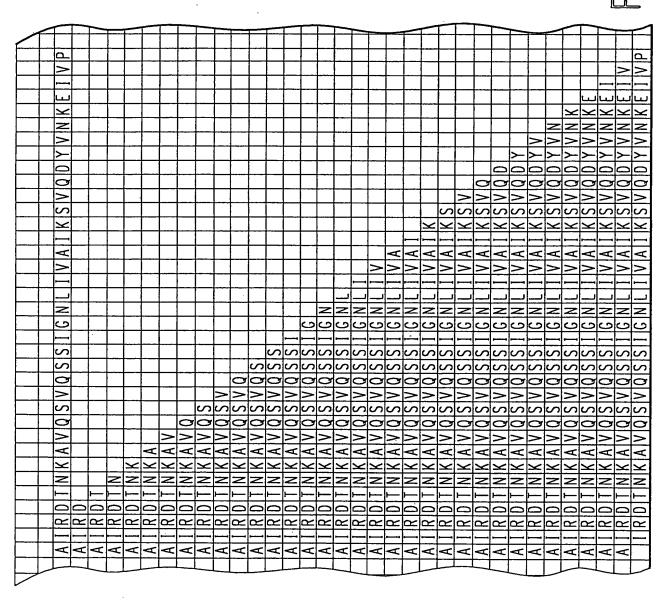
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Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

1G. 29B





Docket No.: 7872-027-999

Serial No.: 08/487,355
Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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FIG.29C



Docket No.: 7872-027-999
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Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

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FIG. 29E

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Docket No.: 7872-027-999

Serial No.: 08/487,355
Inventor(s): Barney et al.
Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

FUSION PEPTIDE

♥ALLMOTI5♥

★107x178x4**★**

.....RNKRGVFVLGFLGFLATAGSAMGAAS ♠♥ XXXXAQSRTLLAGIVQQQQQ

<u>LLDVVKROQELLRLTVWGTKNLQTRVTAIEKYLKDQAQL</u>

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RQVCHTTVPWPNASLTPDW *MND ▼TWQEWERKVDFLEENITALLEEAQIQQ

<u>♦107x178x4</u> EKNMY <u>♦ELQKLNSWD</u>* <u>VF</u>♥ <u>GNXXXXXXXXXXXXXXXXXXXXXXXX</u>

IYIVMLAKLRQGYRPVFSSPPSYFQXTIITQQDPALPTREGKEGDGGEGGGNSSWP WQIEYIHF

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

MTRRRVLSVVVLLAALACRLGAQTPEQPAPPATTVQPTATRQQTSFPFRVCELSSHGDLFRFSSD

♠ 107x178x4
♠

IQCPSFGTRENHTEGLLMVFKDNIIPYSF ♠ KVRSYTKIVTNILIYNGWYADSVTNRHE♠ EKFSVDSY ETDQMDTIYQ CYNAVKMTKD GLTRVYVDRD GVNITVNLKP TGGLANGVRR YASQTELYDA PGWLIWTYRT RTTVNCLITD MMAKSNSPFD FFVTTTGQTV EMSPFYDGKN KETFHERADS FHVRTNYKIV DYDNRGTNPQ GERRAFLDKG TYTLSWKLEN RTAYCPLQHW QTFDSTIATE TGKSIHFVTD EGTSSFVTNT TVGIELPDAF KCIEEQVNKT HEKYEAVQD RYTKGQEAIT YFITSGGLLL AWLPLTPRSL ATVKNLTELT TPTSSPPSSP SPPAPSAARG STPAAVLRRR RRDAGNATTP VPPTAPGKSL GTLNNPATVQ IQFAYDSLRR QINRMLGDLA RAWCLEQKRQ NMVLRELTKI NPTTVMSSIY GKAVAAKRLG DVISVSQCVP VNQATVTLRK SMRVPGSETM CYSRPLVSFS FINDTKTYEG QLGTDNEIFL TKKMTEVCQA TSQYYFQSGN

★107x178x4**★** EIHVYNDYHH FKTIELDGIA TLQTFISLNT ♠SLIENIDFASLELYSRDEQRASNVFD *LE♠

LVS PREDICTED COILED COIL TM Potential GIFREYNFQAQNIAGLRKDLDNAVSN* GRNQ FVDGLGELMDSLGSVG QSITN

♣P12LZIPC♣

TM Potential

TM Potential

LVSTVGGLFSSLVSGFISF FK N &PFGGMLILVLVAGVVILVISL& TRRTRQMS

QQPVQMLYPG IDELAQQHAS GEGPGINPIS KTELQAIMLA LHEQNQEQKR AAQRAAGPSV ASRALQAARDRFPGLRRRRY HDPETAAALL GEAETEF



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

MMDPNSTSED VKFTPDPYQV PFVQAFDQAT RVYQDLGGPS QAPLPCVLWP VLPEPLPQGQ LTAYHVSTAP TGSWFSAPQP APENAYQAYA APQLFPVSDI TQNQQTNQAG GEAPQPGDNS TVQTAAAVVF ACPGANQGQQ LADIGVPQPA PVAAPARRTR KPQQPESLEE CDSELEI

@DNA BINDING@

★107x178X4**★**

+DIMERIZATION+

@KRY KNRVASRKCRAK

★EK@ Q

+LLOHYREVAAAKSSENDRLRLLLKQ♠

MCPSLDVD+ SI IPRTPDVLHE DLLNF

DEC 3 1 2003 THE TRADEMARY CHE

Docket No.: 7872-027-999 Serial No.: 08/487,355 Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

FUSION PEPTIDE

♥ALLMOTI5**♥**

LVS_COILED-COIL

FAG

♥VVLAGAALGVATAAQITAGIALHQSML*NSQAIDNLRASLETTN

<u>OAIEAIROAGOEMI</u>*LAVQGVQDYINN♥ ELIPSMNQLSCDLIGQKLGLKLLRYYT

♣P23LZIPC♣

♣P6,12LZIPC♣

★107X178X4★

♥ALLMOTI5♥

EILSLFGPSLRD ♣PISA ♠♥<u>EISIOLSYALGGDINKV</u>♣ <u>LEKLGYSGGDL</u>♣

♣P1.12LZIPC♣

LGILES♠ RGIKARI♥ THVDTESYFIVLSIAY ♣PTLSEIKGVIVHRLEGV♣ SY

NIGSQEWYTTVPKYVATQGYLISNFDESSCTFMPEGTVCSQNALYPMSPLLQECL

RGSTKSCARTLVSGSFGNRFILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAA

♣P23LZIPC♣

♣P12LZIPC♣

♥ALLMOTI5♥

LVS COILED-COIL

DHCPVVEVNGVTIQVGSRRYPDAVYLHRIDLGP ♣P ♥IS *LERLDVGTNLGN

◆TRANSMEMBRANE REGION◆

AIAKLEDAKELL♣ ESSDOI*L♣ RSMK ♦GLSSTSIVYILI♥ AVCLGGLIGIP

<u>ALICCC</u>♦ RGRCNKKGEQVGMSRPGLKPDLTGTSKSYVRSL



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

Pre S1 and Pre S2
MGQNLSTSNPLGFFPDHQLDPAFRANTANPDWDFNPNKDTWPDANKVGAGAFG
LGFTPPHGGLLGWSPQAQGILQTLPANPPPASTNRQSGRQPTPLSPPLRNTHPQAM
QWNSTTFHQTLQDPRVRGLYFPAGGSSSGTVNPVLTTASPLSSIFSRIGDPALN

MAJOR SURFACE ANTIGEN(HBs)

FUSION

PEPTIDE

♣P12 & 23LZIPC♣

MENITSG FLG ♣PLL VLQAGFFLLTRILTI♣ PQSLDSWWTSLNFLGGTTVCLG

♣P12 & 23LZIPC♣

QNSQSPTSNHSPTSCPPTC ♣PGYRWMCLRRFIIFLFILLLCLIFLLVLLDYQGML♣

PVCPLIPGSSTTSTGPCRTCMTTAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKF

◆TRANSMEMBRANE REGION◆
LWEWASARFSWLS ◆LLVPFVQWFVGLSPTVWLSVI◆ WMMWYWGPSL

- **♦**TRANSMEMBRANE REGION
- **♦YSILSPFLPLLPIFFCLWVYI♦**



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

FUSION ♥ ALLMOTI5 ♥ <u>\$107x 178x4</u>\$

PEPTIDE *LVS COILED COIL

AIQLIPLFVG LGI ♥TTAVSTGAAGLGVS <u>\$IT</u> *QYTKLSHQLISDV

QAISSTIQDLQDQVDSLAEVVLQ* NRRGLDLLTAE♠ QGGI♥

CLALQEKCCFYANKSGIVRDKIKNLQDDLERRRRQLIDNPFWTSFHG

FLPYVMPLLGPLLCLLLVLSFGPIIFNKLMTFIKHQIESIQAKPIQVHYH

TRANSMEMBRANE REGION RLEQEDSGGSYLTLT......????????????????????????....



Inventor(s): Barney et al.

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MKAQKGFTLI ELMIVVAIIG ILAAIAPGQ

<u>**4107x178x4</u>**</u>

∀ALLMOTI5♥

♦♥YODYTARTOYTRAVSEYSALKTAAESAILEGKEIVSSA♦ T**♥**

PK DTQYDIGFT

107x178x4

♥ALLMOTI5♥

▲♥ESTLLDGSGKSQIQVTDNQDGTVELVATLGKSSGS◆ AIKGAVITSR♥

KNDGV WNCKITKTPT AWKPNYAPAN CPKS



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

MNTLQKGFTL IELMIVIAIV GILAAVALPA YQDYTARAQV

SEAILLAEGQ KSAVTEYYLN HGIWP

★107x178x4★

▼<u>ALLMOTI5</u>♥

♦♥KDNTSAGVASSSSIKGKYVKEVKVENGVVTAT

MNSSNVNKEIQGKKLSLWAKRQDGSVKW♥

FCGQP VTRNAKDDTV TADATGNDGK IDTKHLPSTC RDNFDAS

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

MKKTLLGSLI LLAFAGNVQA DINTETSGKV TFFGKVVENT

CKVKTEHKNL SVVLNDVGKN SLSTKVNTAM PTPFTITLQN

CDPTTANGTA NKANKVGLYF Y

\$107x178x4\$ **\$ALLMOTI5**\$ **\$SWKNYDKENNFTLKNEOTTADYATNYNI**\$

QLMESNGTKAISVVGKETE

DF MHTNNNGVAL NQTHPNNAHI SGSTQLTTGT NELPLHFIAQ

YYATNKATAG KVQSSVDFQI AYE

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

MNKKLLMNFF IVSPLLLATT ATDFTPVP

≙107x178x4♀ ♥ALLMOT15♥

 $\diamondsuit \heartsuit \underline{LSSNQIIKTAKASTNDNIKDLLDWYSSGSDTFTNS} \diamondsuit \heartsuit$

EVLDNSL GSMRIKNTDG SISLIIFPSP YYSPAFTKGE KV

N TEKLPTPIEL PLKVKVHGKD SPLKYG

HGLYRSSDKT GGYWKITMND GSTYQSDLSK KFEYNTEKPP

INIDEIKTIE AEIN

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

MKKTAFILLL FIALTLTTSP L

♥ALLMOTI5♥ ♥VNG

★107x178x4★

- *LVS PREDICTED COILED-COIL*
- *S <u>♦EKSEEINEKDLRKKSELQRNALSNLRQIY</u>* <u>YYNEKAITENKESDD</u>

QFLENTLL♥ FKG FFTGHPW

- **±107x178x4±**
- **<u>♦YNDLLVDLGSKDATNKYKGKKVDLYGAY</u>**

YGYQCAGGTPNKTACMYGGVTLHDN NRLTEEKKVP INLWIDGKQTTV

- **♣**P12LZIPC**♣**
- **♣**PIDKVKTSKKEVTVQELDL**♣** QARHYLHGK FGLYNSDSFGGKVQ

♣P12LZIPC**♣**

RGLIVF HSSEGSTVSY DLFDAQGQY ♣P DTLLRIYRDN KTINSENLHI♣

DLYLYTT



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

♥ALLMOTI5**♥**

MKKTAFTLLL FIALTLTTSP L ♥VNGS

- **★107x178x4★**
- **♠EKSEEINEKDLRKKSELQGTALGNLKQIYYYNEKAKTENKESHD♠ Q♥**

FLQHTILFKG FFTDHSWYND LLVDFDSKDI VDKYKGKKVDLYGAYY

GYQC AGGTPNKTAC MYGGVTLHDN NRLTEEKKVPINL WLDGKQNTV

★107x178x4**★**

- **♥**ALLMOTI5♥
- **♣P12LZIPC**♣
- ♣P ♥L ♠ETVKTNKKNVTVQELDLQARRYL♣ QEKYNLYN♠

SDVFDGKVQR♥ GLIVF HTSTE

- ♣P23LZIPC♣
- **♣**PSVNYDLFGAQGQYSNTLLRIYRDNKTINSENMIII**♣** DIYLYTS



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

MKNITFIFFILLASPLYANGDRLYRADSRPPDEIKRFRSLMPRGNEYFDRGT

♥ALLMOTI5♥ ♥QMNINLYDHARGTQTGFVRYDDGYV

SP HPYEQEVSAL GGIPYSQIYG WYRVNFGVID ERLHRNREYR

DRYYRNLNIA PAEDGYRLAG FPPDHQAWRE EPWIHHAPQG

CGDSSRTITG DTCNE

♥ALLMOTI5♥ ♥ETQNLSTIYLREYQSKVKRQIFSDYQSEVDIYNRIRDEL♥



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"

MMFSGFNADY EASSSRCSSA SPAGDSLSYY HSPADSFSSM GSPVNAQDFC TDLAVSSANF IPTVTAISTS PDLQWLVQPA LVSSVAPSQT RAPHPFGVPA PSAGAYSRAG VVKTMTGGRA

LVS PREDICTED COILED-COIL
QSIGRRGKVE QLSPEEEEKR RIRRE *RNKMA AAK

±107x178x4**±**

♥ALLMOTI5♥

♥CRNRRREL <u>★TDTLQAETDQLEDEKSALQTEIANLLKEKEKL</u>♥

EFILAAHR* PACKIPDDL GFPEEMSVAS LDLTGGLPEV
ATPESEEAFT LPLLNDPEPK PSVEPVKSIS SMELKTEPFD
DFLFPASSRP SGSETARSVP DMDLSGSFYA LPLLNDPEPK
PSVEPVKSIS SMELKTEPFD DFLFPASSRP SGSETARSVP
DMDLSGSFYA GSSSNEPSSD SLSSPTLLAL

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EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

SGWESYYKTEGDEEAEEEQEENLEASGDYKYSGRDSLIFLVDASKA MFESQSEDELTPFDMSIQCIQSVYISKIISSDRDLLAVVFYGTEKDKNS VNFKNIYVLQELDNPGAKRILELDQFKGQQGQKRFQDMMGHGSDY SLSEVLWVCANLFSDVQFKMSHKRIMLFTNEDNPHGNDSAKASRAR TKAGDLRDTGIFLDLMHLKKPGGFDISLFYRDIISIAEDED

★107x178x4★

♥ALLMOTI5**♥**

LVS PREDICTED COILED-COIL

♥LRVH *FEE ♠SSKLEDLLRKVRAKETRKRALSRLKLKLNKDIV* ISV

GIYNLVQKAL♥ KPPPIKLYRETN♠ EPVKTKTRTFNTSTGGLLLPSDTKR

SQIYGSRQIILEKEETEELKRFDDPGLMLMGFKPLVLLKKHHLRPSLFVYPE ESLVIGS STLFSALLIKCLEKEVAALCRYTPRRNIPPYFVALVPOEEELDDOK IQVTPPGFQLVFLPFADDKRKMPFTEKIMATPEQVGKMKAIVEKLRFTYRS DSFENPVLQQHFRNLEALALDLME

♣PI2LZIPC♣

♣PEQAVDLTLPKVEAMNKRL♣ GSLVDEFKELVYPPDYNPEGKVTKR KHDNEGSGSKRPKVEYSEEELKTHISKGTLGKFTVPMLKEACRAYGLKSG LKKQELLEALTKHFQD



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GGGALSPQHSAVTQGSIIKNKEGMDAKS

★107x178x4★

♥ALLMOTI5♥

▼▲LTAWSRTLYTFKDYFYDFTREEWKLLDT AQQIVYRNV
MLENYKNLVSLGYQLT KPDVILRLEKGEEPWLVEREIHQETHPD
SETAFEIKSSVSSRSIFKDKQSCDIKMEGMARNDLWYLSLEEVWKCR
DQLDKYQENPERHLRHQLIHTGEKPYECKECGKSFSRSSHLIGHQKT
HTGEEPYECKECGKSFSWFSHLVTHQRTHTGDKLYTCNQCGKSFVH
SSRLIRHQRTHTGHKPYECPECGKSFRQSTHLILHQRTHVRVRPYECN
ECGKSYSQRSHLVVHHRIHTGLKPFECKDCGKCFSRSSHLYSHQRTH
TGEKPYECHDCGKSFSQSSALIVHQRIHTGEKPYECCQCGKAFIRKN
DLIKHQRIHVGAETYKCNQCGIIFSQNS

♣P23LZIPC♣

♣PFIVHQIAHTGEQFLTCGNQCGTALVNTSNLIGQTNHI**♣** RENAY



Docket No.: 7872-027-999
Serial No.: 08/487,355
Inventor(s): Barney et al.
Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

RESIDUE — 438 PO AVYLHRI DLG PP I SLERL DVG TNLC NAIAKLE AKELLE S S DO I LR S M -488 # 1			_																			
MACASES ED. 178-116E WALK	\vdash																					
WEASLES FD. 178-LIKE WALK								\square														
WEASLES FD. 178-LIKE WALK	8				\Box			_		_			_	_				_				
WEASLES FD. 178-LIKE WALK	4						_				_			_	-		_					
MEASLES ED. 178-LIKE WALK PID A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E D A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E A V Y L H R I D L G P P I S L E R L D V G T N L G N A I A K L E C C P P I S L E R L D V G T N L G N A I A K L E C C P P I S L E R L D V G T N L G N A I A K L E C C P P I S L E R L D V G T N L G N A I A K L E C C P P I S L E R L D V G T N L G N A I A K L E C C P P I S L E R L D V G T N L G N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C N A I A K L E C C C C N A I A K L E C C C C N A I A K L E C C C C N A I A K L E C C C C N A I A K L E C C C C C C C C C C C C C C C C C C					-			\dashv	\dashv	\dashv			-				-	\dashv			=	씈
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Docket No.: 7872-027-999

Serial No.: 08/487,355
Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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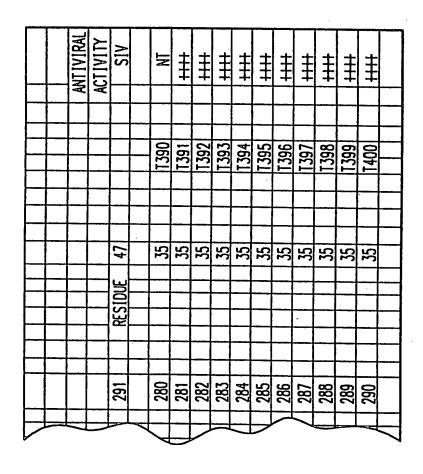
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Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS <u>TRANSMISSION</u>"





Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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FIG. 49A

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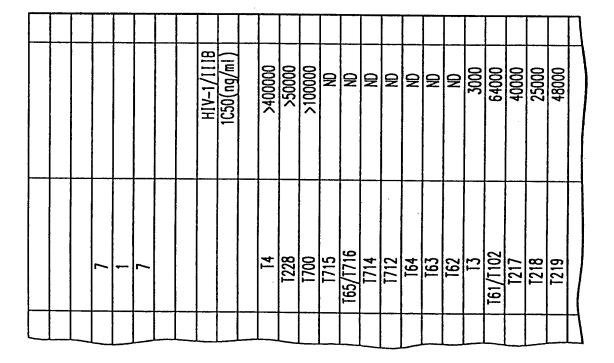
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Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

FIG. 49F





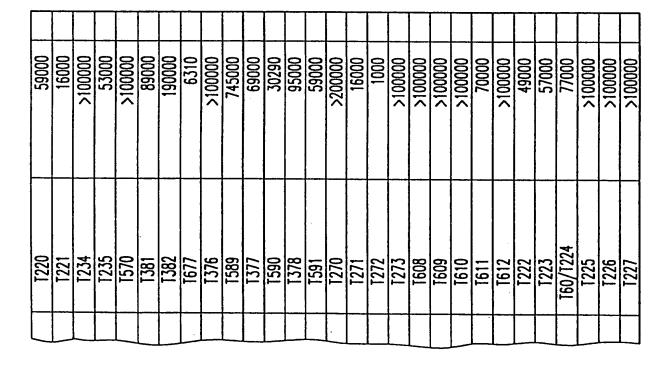
Docket No.: 7872-027-999
Serial No.: 08/487,355
Inventor(s): Barney et al.
Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

FIG 49H





Docket No.: 7872-027-999
Serial No.: 08/487,355
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Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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Docket No.: 7872-027-999 Serial No.: 08/487,355

Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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FIG.51B



Inventor(s): Barney et al.

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION"

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FIG.51C



Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

EVENTS, INCLUDING HEPATITIS B VIRUS TRANSMISSION



174 P-L-L-V-L-Q-A-G-F-F-L-L-I-R-I-L-I-P-Q-S-L-D-S-W-W-I-S-L-N-F-L-G-G-I-T-V-C-L-G-Q-N-S-Q-S-P₂₁₉ DOMAIN I

[-T-1-K-1-T-1-1-P-Q-S-L-D-S-W-N-1-S-L-N-F-L-G-G-1-1-N-C-L-G-Q-N-S-Q-S F-L-L-1-R-1-L-1-1-P-Q-S-L-D-S-W-W-1-S-L-N-F-L-G-G-1-1-V-C-L-G-Q-N-S-(F-F-L-L-1-R-1-L-1-1-P-Q-S-L-D-S-W-W-1-S-L-N-F-L-G-G-1-1-V-C-L-G-Q-N-S G+F+L-L-1-R-1-L-1-1-P-Q-S-L-D-S-W-W-1-S-L-N-F-L-G-G-1-1-V-C-L-G-Q-N Q-A-G-F-F-L-L-1-R-1-L-1-1-P-Q-S-L-D-S-W-W-1--S-L-N-F-L-G-G-1-1-V-C-L-C L-Q-A-G-F-F-L-L-T-R-I-L-I-I-P-Q-S-L-D-S-W-W-I-S-L-N-F-L-G-G-I-I-V-C-V-L-Q-A-G-F-F-L-L-T-R-I-L-I-I-P-Q-S-L-D-S-W-W-I-S-L-N-F-L-G-G-I-I-V-(L-V-L-Q-A-G-F-F-L-L-T-R-1-L-I-1-Q-S-L-D-S-W-W-T-S-L-N-F-L-G-G-T--I-L-L-V-L-Q-A-G-F-F-L-L-T-R-I-L-T-I-P-Q-S-L-D-S-W-W-T-S-L-N-F-L-G-G-T-I P-L-L-V-L-Q-A-G-F-F-L-L-T-R-I-L-T-I-P-Q-S-L-D-S-W-W-T-S-L-N-F-L-G-G-I

FIG.52A

Title: "METHODS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED

Y-R-W-M-C-L-R-R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V G-Y-R-W-M-C-L-R-R-F-I-I-F-L-F-I-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P P-G-Y-R-W-M-C-L-R-R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L

DOMAIN II

R-W-M-C-L-R-R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C

W-M-C-L-R-R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P

M-C-L-R-R-F-I-I-F-L-F-I-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L

L-R-R-F-I-I-F-L-F-I-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P C-L-R-R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I

F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S R-R-F-I-I-F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G

L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G F-L-F-I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T

I-L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G-P-C F.I.L.L.L.C.L.I.F.L.L.V.L.L.D.Y.Q.G.M.L.P.V.C.P.L.I.P.G.S.S.T.T.S.T.G.P

L-L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G-P-C-R

L·C·L·I·F·L·L·V·L·L·D·Y·Q·G·M·L·P·V·C·P·L·I·P·G·S·S·T·T·S·T·G·P·C·R·T·C L-L-C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G-P-C-R-T

L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G-P-C-R-T-C-M-T C-L-I-F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G-P-C-R-T-C-M

I.F-L-L-V-L-L-D-Y-Q-G-M-L-P-V-C-P-L-I-P-G-S-S-T-T-S-T-G-P-C-R-T-C-M-T-T

FIG.52B